

REMARKS

This is in response to the Office Action dated June 20, 2005. Claims 17-18, 24, 29, 34, 41, 43, 45, 47, 48, and 54 have been canceled without prejudice to filing in a later application. Claim 51 was canceled because it was a duplication of Claim 50. Claims 1, 38, and 39 have been amended. Claims 1-16, 19-23, 25-28, 30-33, 35-40, 42, 44, 46, 49-50, 52-53, and 55-59 are now pending.

I. Rejection under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claims 1-59 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

To expedite prosecution, applicant has amended independent claim 1 to clarify that the claims amount of 0.5-50% refers to a w/w concentration of the edible wax in the composition, and cancel claims 24, 29, 34, 39, 41, 43 and 45. Withdrawal of the rejection is therefore respectfully requested.

II. Rejection under 35 U.S.C. § 102

The Examiner rejects Claims 1-11, 13-14, 17-18, 20-21, 23-26, 28-31, 33-35 and 38-56 under 35 USC 103(a) as being anticipated by Xu (US 5405608 A).

Independent claim 1 as amended specifies a composition comprising edible oil, edible wax and sterol compound that are homogenized to form a colloid with the edible wax adopting **microcrystal form** at ambient temperature. Support for the claim language appears, for example, in claim 48 as originally filed, and in paragraph 00139 in the specification. As described in detail in EXAMPLE 1 of the specification, the mixture of edible oil, edible wax and sterol compound was homogenized or ground in a colloid mill at $40 \pm 2^{\circ}\text{C}$ for certain time to

produce a colloid form of composition with the edible wax adopting microcrystal form upon cooling to ambient temperature.

In contrast, Xu discloses a simple mixture of edible oil, wax, sterol, etc., which was produced by mixing the components at 180°C for 30 min without going through homogenization. Column 6, lines 5-14.

In fact, the instant application has compared the physical characteristics of the topical formulation used for treating thermal injury in Xu with the inventive oral formulation. As described in the specification in paragraph 00137, an edible wax, for example beeswax, usually has a higher melting point than the edible oil (e.g., sesame oil). Beeswax is solid at room temperature and melts when heated to about 70-80°C. Thus, at 180°C the wax was completely liquefied; and when a liquefied wax and an edible oil (e.g., sesame oil) are mixed without going through homogenization, because the wax cools down much faster than the oil due to their differential thermo-physical properties, the solidified wax forms a 3-dimensional structure with small "pigeonholes" within which oil drops are enclosed. In the specification Figure 4A illustrates a model structure with beeswax forming the pigeonholes and oil drops enclosed therein. Figure 4B shows an electronograph of a mixture comprising about 10% beeswax and about 90% sesame oil. As shown in Figure 4B, beeswax forms a three-dimensional pigeonhole-like structure with the dimension of the holes averaged at 19 μm and has individual oil drops enclosed therein.

In contrast, when the mixture of beeswax and sesame oil is homogenized by emulsification, for example, with a homogenizer or a colloid mill, the homogenized mixture of beeswax and sesame oil appears to adopt a colloidal form. Examined under a microscope at ambient temperature, discrete microcrystals of beeswax form and distribute more or less uniformly through out the texture. Figures 5A-B are micrographs showing the microcrystals of beeswax in an embodiment of the composition comprising about 7% of beeswax homogenized with about 92% of sesame oil. As shown in Figures 5A-B, there are two major forms of the microcrystals: needle-like microcrystals (Figure 5A) and microcrystal complexes in bundles or in various asterisk shapes (Figure 5B). In contrast to the mixture show in Figure 4B where oil drops are enclosed in the "pigeonhole" structure formed by beeswax, here microcrystals of

beeswax are dispersed in the oil quite uniformly without forming a connected 3D network structure.

In view of the distinct differences in physical characteristics of the topical formulation disclosed in Xu and the claimed invention, Applicants submit that the pending claims are not anticipated by the cited reference under 35 U.S.C. §102(b). Withdrawal of the rejection is therefore respectfully requested.

III. Rejection under 35 U.S.C. § 103

1. Over Xu

Claims 1, 21-23, 26-27, 31-32, and 36-37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Xu.

As discussed in detail above, the claimed oral formulation has distinctively different physical characteristics from those of the topical formulation disclosed in Xu. Further, microcrystals in the colloid form of the inventive formulation better adhere to the gastric mucosa than the pigeonhole structure of the topical formulation in Xu. Since the melting point of beeswax is 70-80°C whereas the temperature in the stomach is about 37°C, it would be physically infeasible to convert the already solidified wax structure to a colloid form in the stomach without first being ground by a homogenizer or colloid mill ex vivo. Due to its superior ability to adhere to the gastric mucosa, Applicants demonstrated that an embodiment of the inventive formulation is much more efficacious in protecting animals from developing acute gastric ulcer. As described in page 35, in vivo studies of animal models for acute ulcer caused by alcohol demonstrated that the formulation wherein beeswax adopts the pigeonhole structure (Figure 4B) could not effectively protect rats from developing gastric ulcer with just one time administration of the composition to the rats. In contrast, the inventive formulation with microcrystals of beeswax distributing evenly through out the colloidal texture was very effective in preventing ulcer development in the rats with just one time administration of the composition. These results indicate that the inventive formulation with the wax homogenized with the oil is particularly

effective in adhering to mucosa in the GI tract and protecting it from the ulcerous effects of alcohol. In comparison, the composition wherein beeswax adopts the pigeonhole structure with oil drops enclosed (as that disclosed in Xu) is presumed to adhere poorly and/or too slowly to the gastric mucosa before being exposed to alcohol.

Nowhere does Xu teach or suggest that a simple mixture of edible oil, wax, sterol, etc. should be subject to homogenization or colloid milling at a temperature lower than 180°C. To the contrary, a topical formulation adopting a pigeonhole structure with oil drops enclosed therein is probably more desirable for faster wound healing of the skin as it allows removal of the excreta from the wound through the holes in the network of beeswax. Column 3, lines 54-59.

To establish a prima facie case of obviousness, the Examiner bears the burden of proving 1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; 2) the prior art contains a suggestion or motivation to combine the prior art references in such a way as to achieve the claimed invention; and 3) one of ordinary skill in the art at the time the invention was made would have reasonable expectation of success of the claimed invention. *In re Vaeck*, 947 F. 2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *In re O'Farrell*, 853 F. 2d 894, 903-904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); and *In re Dow Chem.*, 837 F. 2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

Xu's disclosure of a simple mixture of ingredients for topical administration in the treatment of thermal injury gives no clue as to how one would modify it to better adhere to the gastric mucosa and succeed in protecting the mucosa from assaults such as excessive alcohol. Thus, this cited reference not only fails to teach the invention, but also fails to suggest or to motivate one of ordinary skill in the art to modify it to arrive at the present invention. Thus, the claimed invention is not only novel but also non-obvious over Xu under 35 U.S.C. §103(a). Withdrawal of the rejection is therefore respectfully requested.

2. Over Chen et al.

Claims 1-11, 13-16, 48-53 and 55-59 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 6,306,435 B1).

As discussed in detail above, the claimed oral formulation has distinctive physical characteristics. Specifically, microcrystals in the colloid form of the inventive formulation better adhere to the gastric mucosa than other formulation, such as the one with a pigeonhole structure of wax in the topical formulation in Xu.

Chen does not teach the problem associated with mixing oil and wax without homogenization, let alone suggest any solution to the problem. Further away from the disclosure of Xu, Chen merely teaches in general that the oil matrix is "any oily or greasy substance" (column 5, lines 17-19) but fails to teach or suggest the claimed oral formulation which is colloid with edible oil homogenized with edible wax and a sterol compound at concentrations specified in independent claim 1.

In view of the failure of Chen to teach or suggest the claimed invention, a prima facie case of obviousness has been established under 35 U.S.C. §103(a). Withdrawal of the rejection is therefore respectfully requested.

3. Over Chen and Sosnowski

Claims 1 and 12 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chen and Sosnowski (US 4,382,886).

As discussed above, Chen failed to teach or suggest an oral formulation claimed oral formulation which is colloid with edible oil homogenized with edible wax and a sterol compound at concentrations specified in independent claim 1. Further Sosnowski fails to supply the missing elements in Chen that are required for the establishment of a prima facie case of obviousness under 35 U.S.C. §103(a), as Sosnowski merely discloses adding propolis to an oral composition (see Abstract). Withdrawal of the rejection is therefore respectfully requested.

4. Over Chen and Niazi

Claims 1, 21-36, 40-41 and 44-45 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chen and Niazi (US 6,365,198 B1).

As discussed above, Chen failed to teach or suggest an oral formulation claimed oral formulation which is colloid with edible oil homogenized with edible wax and a sterol compound

at concentrations specified in independent claim 1. Further Niazi fails to supply the missing elements in Chen that are required for the establishment of a prima facie case of obviousness under 35 U.S.C. §103(a). Instead, Niazi teaches that pharmaceutical grade wax is mixed with oil and "the mixture [is] **stirred gently for about 5 minutes** at elevated temperature and the allowed to cool in appropriate containers". Emphasis added, Column 7, lines 21-26.

In view of the failure of Chen and Niazi to teach or suggest the claimed invention, a prima facie case of obviousness has been established under 35 U.S.C. §103(a). Withdrawal of the rejection is therefore respectfully requested.

5. Over Chen and Nakamura

Claims 1, 17,18 and 20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chen and Nakamura et al. (JP 09208598).

As discussed above, Chen failed to teach or suggest an oral formulation claimed oral formulation which is colloid with edible oil homogenized with edible wax and a sterol compound at concentrations specified in independent claim 1. Further, Nakamura fails to supply the missing elements in Chen that are required for the establishment of a prima facie case of obviousness under 35 U.S.C. §103(a), as Nakamura et al. merely discloses adding betasitosterol to a composition for treating gastrointestinal disorders (see Abstract). Withdrawal of the rejection is therefore respectfully requested.

6. Over Chen, Nakamura and Kitano

Claims 1 and 17-19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chen, Nakamura and Kitano (JP 61050919).

As discussed above, both Chen and Nakamura fail to teach or suggest an oral formulation claimed oral formulation which is colloid with edible oil homogenized with edible wax and a sterol compound at concentrations specified in independent claim 1. Further, Kitano fails to supply the missing elements in Chen and Nakamura that are required for the establishment of a prima facie case of obviousness under 35 U.S.C. §103(a), as Kitano merely discloses adding phytosterol to a composition for treating gastrointestinal disorders (see Abstract). Withdrawal of

the rejection is therefore respectfully requested.

IV. Double Patenting

Claims 1-11, 13-14, 17-18, 20-56 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of Xu (U.S. Patent No. 5,405,608).

Independent claim 1 as amended specifies an **oral** formulation comprising edible oil, edible wax and sterol compound that are homogenized to form a colloid with the edible wax adopting **microcrystal form** at ambient temperature.

In contrast, claims 1-3 of Xu are directed to a **topical** formulation comprising a mixture of beeswax, sesame oil and various other ingredients. As discussed in sections II and III above, the claimed invention is not only novel but non-obvious over Xu' topical formulation for treating thermal injury. Xu neither teaches nor suggests a colloid form of composition with the edible wax adopting microcrystal form. Instead, Xu discloses a simple mixture of edible oil, wax, sterol, etc., which was produced by mixing the components at 180°C for 30 min without going through homogenization. Column 6, lines 5-14. In absence of such teaching or suggestion, the claimed invention is not rendered obvious by claims 1-3 of Xu. Withdrawal of the rejection is therefore respectfully requested.

Application No. 10/669,094
Response dated October 7, 2005
Reply to Office Action dated June 20, 2005

Conclusion

In light of the remarks and arguments set forth above, Applicant earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner believe that any additional information or documentation is necessary to place the application in condition for allowance, she is urged to contact the undersigned Attorney via telephone at 650-565-3856.

The Commissioner is hereby authorized to charge any required fees due in connection with this submission and to credit any overpayment, to Deposit Account No. 23-2415 (Docket No. 27348-702.401).

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

Dated: October 7, 2005

By



Shirley Chen, Ph.D.
Registration No. 44,608

650 Page Mill Road
Palo Alto, California 94304-1050
Direct Dial: (650) 565-3856
Fax No.: (650) 493-6811

Customer No. 021971